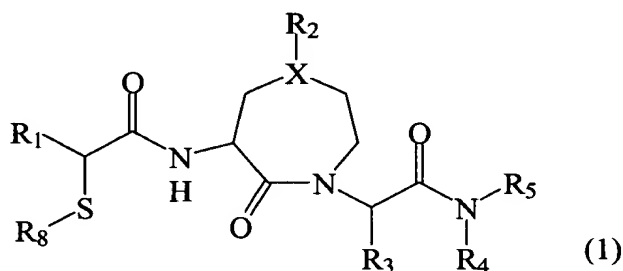


LISTING OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) A compound of the formula



wherein

R₁ is C₁-C₆ alkyl, a W-(CH₂)_m- group, or a Q-Z-(CH₂)_m- group wherein W is phthalimido; Z is a bond or is oxy, NR₆, C(O)NR₆, NR₆C(O), NHC(O)NR₆, OC(O)NR₆, HNC(O)O, or SO₂NR₆; Q is hydrogen, or a Y-(CH₂)_n- group wherein Y is hydrogen, C₆-C₁₀ aryl, ~~C₃-C₉ heteroaryl~~ a cyclic or bicyclic, aromatic assemblage of three to nine carbon atoms and from 1 to 3 nitrogen, oxygen, or sulfur atoms, -C(O)OR₆, -N(R₆)₂, morpholino, piperidino, pyrrolidino, or isoindolyl;

R₂ is C₁-C₄ alkyl, a -(CH₂)_p-(C₃-C₉)heteroaryl group, or a -(CH₂)_p-Ar₁ group wherein Ar₁ is phenyl or naphthyl optionally substituted with a substituent selected from the group consisting of halogen, C₁-C₄ alkyl, -OR₇, -N(R₆)₂, SO₂N(R₆)₂ or -NO₂;

R₃ is hydrogen, C₁-C₆ alkyl, -CH₂SCH₂NHCOCH₃, a -(CH₂)_p-A group, a -(CH₂)_m-B group or a -CH₂-D-R₇ group wherein A is C₆-C₁₀ aryl, C₃-C₉ heteroaryl, or cyclohexyl; B is -N(R₇)₂, guanidino, nitroguanidino, -C(O)OR₆ or -C(O)NR₆; and D is oxy or thio;

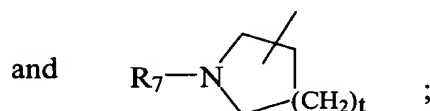
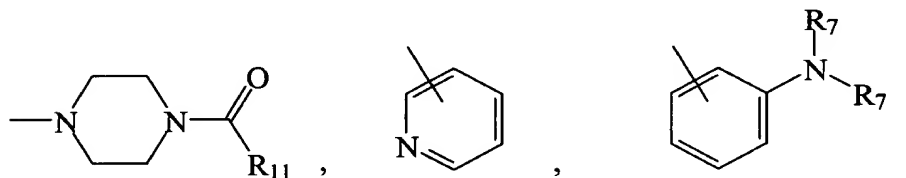
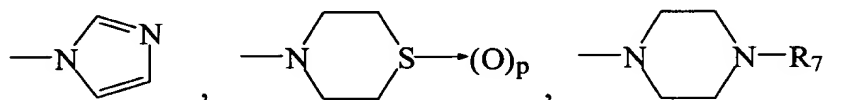
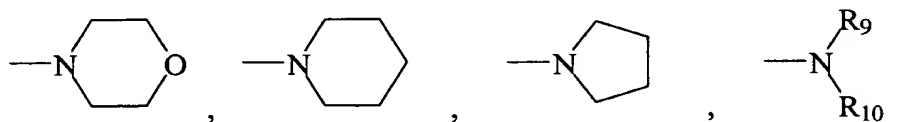
R₄ is hydrogen or a -(CH₂)_m-S(O)_pX'(R₆)₂ group;

R_5 is hydrogen, C_1 - C_6 alkyl or R_4 and R_5 taken together with the nitrogen atom to which they are attached form piperidino, pyrrolidino, or isoindolyl;

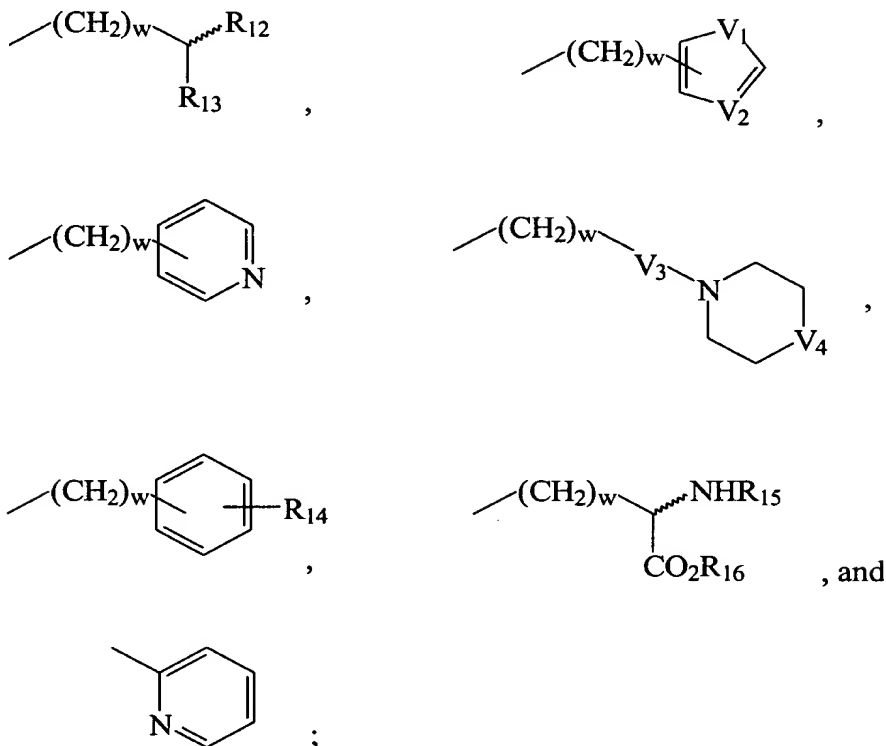
R_6 is hydrogen or C_1 - C_6 alkyl;

R_7 is hydrogen, C_1 - C_4 alkyl, or a $-(CH_2)_p$ - Ar_2 group wherein Ar_2 is phenyl or naphthyl optionally substituted with a substituent selected from the group consisting of halogen, C_1 - C_4 alkyl, $-OR_7$, $-N(R_6)_2$, $SO_2N(R_6)_2$ or $-NO_2$;

R_8 is hydrogen, $-C(O)R_7$, a $-C(O)-(CH_2)_q$ -K group or a $-S-G$ group, wherein K is selected from the group consisting of



G is selected from the group consisting of



R_9 and R_{10} are each independently C_1 - C_4 alkyl or a $-(\text{CH}_2)_p\text{-Ar}_2$ group;

R_{11} is $-\text{CF}_3$, C_1 - C_{10} alkyl or a $-(\text{CH}_2)_p\text{-Ar}_2$ group;

R_{12} is hydrogen, C_1 - C_6 alkyl, $-\text{CH}_2\text{CH}_2\text{S}(\text{O})_p\text{CH}_3$, or arylalkyl;

R_{13} is hydrogen, hydroxy, amino, C_1 - C_6 alkyl, N-methylamino, N,N-dimethylamino,

$-\text{CO}_2\text{R}_{17}$ or $-\text{OC}(\text{O})\text{R}_{18}$ wherein R_{17} is hydrogen, $-\text{CH}_2\text{O}-\text{C}(\text{O})\text{C}(\text{CH}_3)_3$, C_1 - C_4 alkyl, a

$-(\text{CH}_2)_p\text{-Ar}_2$ group or diphenylmethyl and R_{18} is hydrogen, C_1 - C_6 alkyl or phenyl;

R_{14} is 1 or 2 substituents independently chosen from the group consisting of hydrogen,

C_1 - C_4 alkyl, C_1 - C_4 alkoxy, or halogen;

R_{15} is hydrogen, C_1 - C_6 alkyl or a $-(\text{CH}_2)_p\text{-Ar}_2$ group;

R_{16} is hydrogen or C_1 - C_4 alkyl;

V_1 is O, S, or NH;

V₂ is N or CH;

V₃ is a bond or -C(O)-;

V₄ is -(CH₂)_w-, O, S, NR₇, or NC(O)R₁₁;

X and X' are each independently CH or N;

m is an integer 2-4;

n is zero or an integer 1-4;

p is zero or an integer 1-2;

q is zero or an integer 1-5;

t is an integer 1-2;

w is an integer 1-3; and

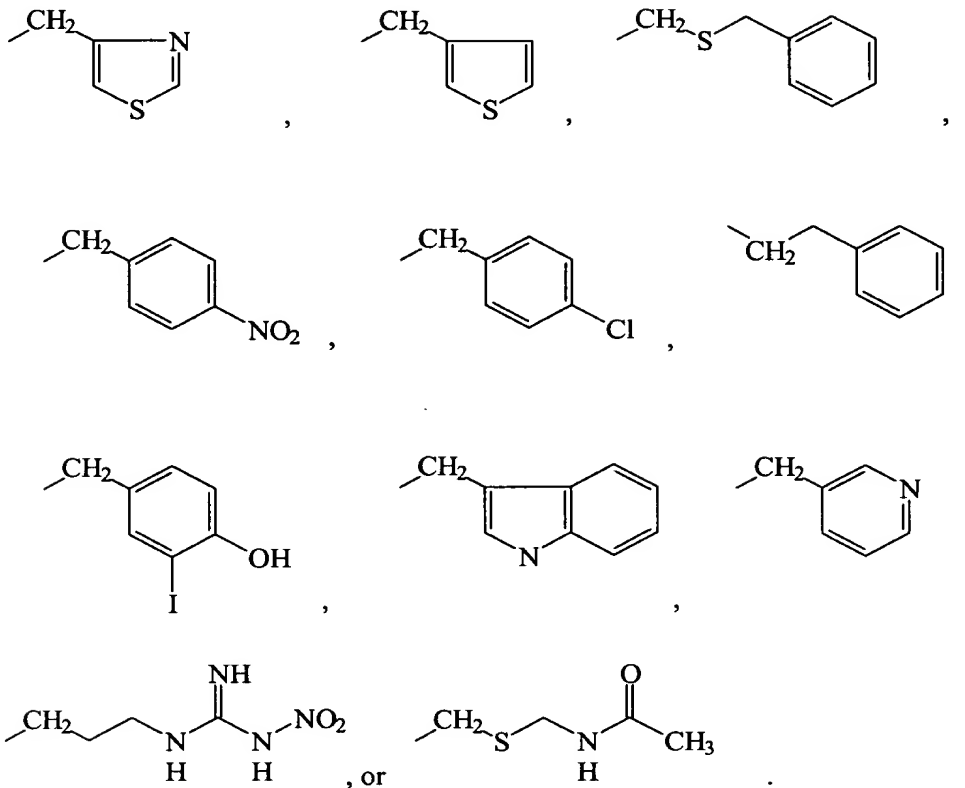
w' is zero or an integer 1; or

a pharmaceutically acceptable salt, stereoisomer or hydrate thereof.

2. (Original) A compound of claim 1 wherein X is CH.

3. (Original) A compound of claim 2 wherein R₂ is C₁-C₄ alkyl or a -(CH₂)_p-Ar group wherein Ar is phenyl optionally substituted with F, Cl, C₁-C₄ alkyl, -NO₂, -NH₂ or -OR₇; and R₄ is hydrogen.

4. (Previously Presented) A compound of claim 3 wherein R₃ is hydrogen, C₁-C₆ alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl, or is a compound of the formula



5. (Original) A compound of claim 4 wherein R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

6. (Original) A compound of claim 2 wherein R_1 is a $W-(CH_2)_m$ - group.

7. (Original) A compound of claim 3 wherein R_1 is a $W-(CH_2)_m$ - group.

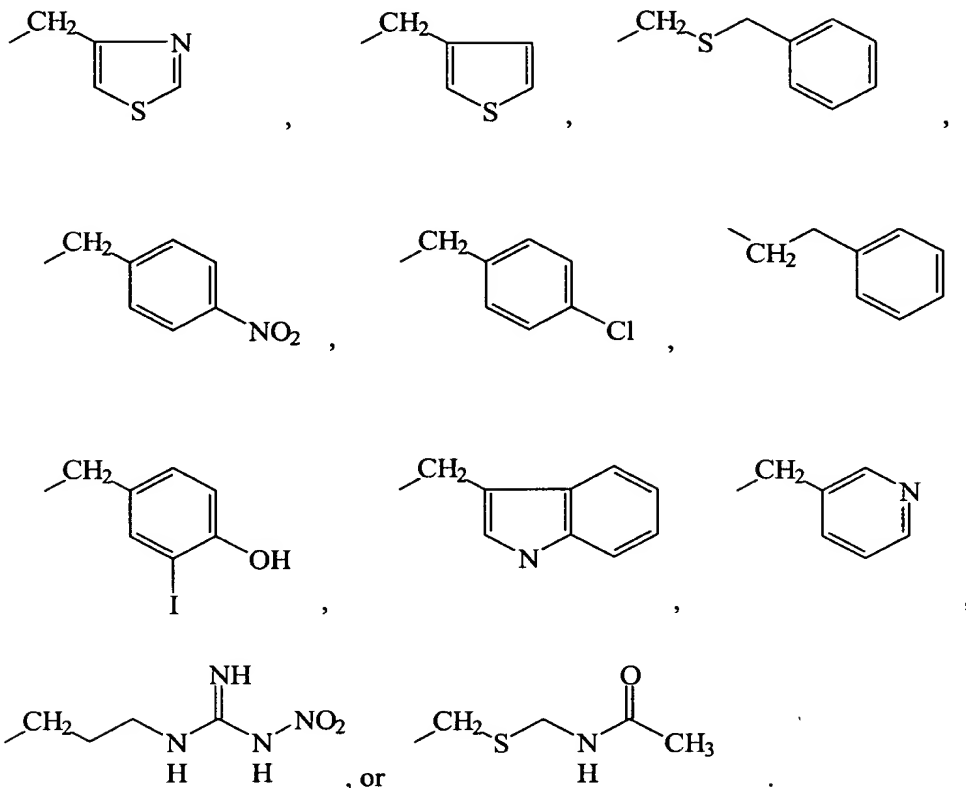
8. (Original) A compound of claim 5 wherein R_1 is a $W-(CH_2)_m$ - group.

9. (Original) A compound of claim 2 wherein R_1 is C_1 - C_6 alkyl.

10. (Original) A compound of claim 3 wherein R_1 is C_1 - C_6 alkyl.

11. (Original) A compound of claim 5 wherein R_1 is a C_1 - C_6 alkyl.

12. (Original) A compound of claim 2 wherein R_1 is a $Q-Z-(CH_2)_m$ -group.
13. (Original) A compound of claim 3 wherein R_1 is a $Q-Z-(CH_2)_m$ -group.
14. (Original) A compound of claim 5 wherein R_1 is a $Q-Z-(CH_2)_m$ -group.
15. (Original) A compound of claim 1 wherein X is N.
16. (Original) A compound of claim 15 wherein R_2 is C_1 - C_4 alkyl or a $-(CH_2)_p$ -Ar group wherein Ar is phenyl optionally substituted with F, Cl, C_1 - C_4 alkyl, $-NO_2$, $-NH_2$ or $-OR_8$; and R_4 is hydrogen.
17. (Previously Presented) A compound of claim 16 wherein R_3 is hydrogen, C_1 - C_6 alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl, or is a compound of the formula



18. (Original) A compound of claim 17 wherein R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

19. (Original) A compound of claim 16 wherein R_1 is a $W-(CH_2)_m$ -group.

20. (Original) A compound of claim 17 wherein R_1 is a $W-(CH_2)_m$ -group.

21. (Original) A compound of claim 19 wherein R_1 is a $W-(CH_2)_m$ -group.

22. (Original) A compound of claim 16 wherein R_1 is C_1 - C_6 alkyl.

23. (Original) A compound of claim 17 wherein R_1 is C_1 - C_6 alkyl.

24. (Original) A compound of claim 19 wherein R_1 is a C_1 - C_6 alkyl.
25. (Original) A compound of claim 16 wherein R_1 is a $Q-Z-(CH_2)_m$ -group.
26. (Original) A compound of claim 17 wherein R_1 is a $Q-Z-(CH_2)_m$ -group.
27. (Original) A compound of claim 19 wherein R_1 is a $Q-Z-(CH_2)_m$ -group.
28. (Original) A compound of claim 1 wherein X is CH; R_2 is phenyl, methyl or ethyl; R_3 is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl; R_4 is hydrogen; R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.
29. (Original) A compound of claim 28 wherein R_1 is a $W-(CH_2)_m$ -group.
30. (Original) A compound of claim 1 wherein X is N; R_2 is phenyl, methyl or ethyl; R_3 is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl; R_4 is hydrogen; R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.
31. (Original) A compound of claim 30 wherein R_1 is a $W-(CH_2)_m$ -group.

32. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro- α -mercapto-1,3-dioxo-, [3*S*-[1(*R**), 3 α , 5 α]]-.

33. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro- α -mercapto-1,3-dioxo-, [3*S*-[1(*R**), 3 α , 5 β]]-.

34. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-4-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-oxo-1-(phenylmethyl)-1*H*-1,4-diazepin-6-yl]-1,3-dihydro- α -mercapto-1,3-dioxo-, [6*S*-[4(*R**), 6*R**(*R**)]]-.

35. (Original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

36. (Cancelled)

37. (Cancelled)

38. (Original) A method of treating rheumatoid arthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

39. (Original) A method of treating osteoarthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

40. (Original) A method of treating a chronic inflammatory disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

41. (Cancelled)

42. (Cancelled)

43. (Original) A method of claim 42 wherein said cardiovascular disorder is atherosclerosis.

44. (Original) A method of treating corneal ulceration in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

45. (Original) A method of treating gingivitis or periodontal disease in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

46. (Cancelled)

47. (Original) A method of treating chronic obstructive pulmonary disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.